

Pre-Treatment Procedures

- Animal health procedure: all animals received a clinical examination for ill-health on arrival and a veterinary clinical examination during the acclimatization period.
- 5 ▪ Acclimatization period: at least 3 weeks between animal arrival and start of treatment.

Experimental Design

- Allocation to treatment groups was performed during the acclimatization period using a random allocation procedure based on body weight classes.
- 10 ▪ Animals were assigned to the treatment groups shown in Table 1. The dose levels administered were shown in Table 2.

Administration of the Test/Control ArticlesGroup 1 and 2 Animals

- Method of administration: injection in the left inguinal lymph node.
- 15 Animals were lightly anaesthetized before each administration by an intramuscular injection of ketamine hydrochloride (Imalgene® 500 - Merial, Lyon, France). The same lymph node was injected on each occasion (left side). Each injection was followed by a local disinfection with iodine (Vétédine® - Vétquinol, Lure, France).

20 Group 3

- Route: subcutaneous.
 - Method of administration: bolus injection using a sterile syringe and needle introduced subcutaneously. Four injection sites were used followed by a local disinfection with iodine (Vétédine® - Vétquinol, Lure, France).
- 25 Animals were also lightly anaesthetized before each administration by an intramuscular injection of ketamine hydrochloride (Imalgene® 500 - Merial, Lyon, France) in order to be under the same conditions as groups 1 and 2 animals.

Four injection sites in the dorsal cervical/interscapular regions were used as shown in Table 3.

▪ **ELISPOT Analysis**

An ELISPOT assay was used in order to assess the cell mediated
5 immune response generated in the monkeys in the various treatment groups. In particular, an ELISPOT IFN γ assay was used in order to measure IFN γ production from T lymphocytes obtained from the monkeys in response to gp100 antigens.

10 **Materials and Methods**

Plates: MILLIPORE Multiscreen HA plate / MAHA S45.10 (96 wells).

Capture antibodies: MABTECH monoclonal anti-IFN γ antibodies/G-Z4 1 mg/mL.

Detection antibodies: MABTECH monoclonal anti-IFN γ antibodies/7-B6-1-
15 biotin 1 mg/mL.

Enzyme: SIGMA, Extravidin-PA conjugate/E2636

Substrate: BIORAD, NBT/BCIP - Alkaline phosphatase conjugate substrate kit/ref: 170-64 32.

Coating

20 Place 100 μ L per well of capture antibodies at 1 μ g/mL diluted at 1/1000 in carbonate bicarbonate buffer 0.1M pH 9.6 into the multiwell plate. Incubate overnight at 4°C. Wash 4 times in 1X PBS.

Saturation

Place 200 μ L per well of RPMI supplemented with 10% FCS, non essential
25 amino acids, pyruvate, Hepes buffer and Peni-Strepto. Incubate 2 hours at 37°C.

Test

Cells from the immunized animals are tested against (a) medium alone; (b) pooled peptides at a concentration of 1 mg/mL; and (c) a non specific

stimulus (PMA-Iono). The pooled peptides used in this Example to stimulate IFN- γ production were derived from gp100 and are illustrated in Tables 4 to 7. The final volume of each sample is 200 μ L. Incubate 20 hours at 37°C.

- 5 Wash 4 times in 1X PBS and 0.05% Tween 20.

Detection

Place 100 μ L per well of detection antibodies at 1 μ g/mL diluted in 1/1000 1X PBS, 1% BSA and 0.05% Tween 20. Incubate 2 hours at room temperature. Wash 4 times in 1X PBS and 0.05% Tween 20.

- 10 **Reaction**

Place 100 μ L per well of Extravidin-PA conjugate diluted 1/6000 in 1X PBS, 1% BSA and 0.05% Tween 20. Incubate 45 minutes at room temperature. Wash 4 times in 1X PBS and 0.05% Tween 20.

Substrate Addition

- 15 Place 100 μ L per well of substrate previously prepared. For example, for 1 plate, prepare: 9.6 mL of distilled water, 0.4 mL of 25X buffer, 0.1 mL of solution A (NBT) and 0.1 mL of solution B (BCIP). Incubate 30-45 minutes at room temperature. Wash in distilled water. Dry and transfer to a plastic film. The number of spots are counted using a Zeiss image analyzer. Each
20 spot corresponds to an individual IFN- γ secreting T cell.

Results

- The animals that tested positive on the ELISPOT analysis are shown in Figures 1-4. Overall, the results demonstrate that of the animals tested, 2
25 out of 2 (i.e. 100%) of the animals that received the intranodal administration of the gp100 antigen, and 2 out of 4 (i.e. 50%) of the animals that received the subcutaneous administration of the gp100 antigen had a positive cell mediated immune response.

ELISA Analysis

The ELISA was performed utilizing standard methodology known in the art. Briefly, the human gp100 ("hgp100"; produced in Baculovirus) was diluted in coating buffer (carbonate-bicarbonate, pH9.6) and added to 96 wells at 0.5ug/well. Plates were placed at 4°C overnight. Plates were then washed and blocking buffer (phosphate buffered saline/0.5% Tween 20/1.0% BSA, pH7.2) was added for 2 hours at 37°C. The plates were then washed and the sera was diluted in dilution buffer (phosphate buffered saline/0.5 % Tween 20/ 0.1 BSA, pH7.2). For this study, monkey sera was diluted to 1:800 and "7" serial 3 fold dilutions were done for each sample tested. The human sera controls were diluted to 1:50 in dilution buffer and "7" serial 2 fold dilutions were performed. Each dilution was done in duplicate. The plates were incubated a further 2 hours at 37°C. The plates were washed and the horse radish peroxidase (HRP)-conjugated anti-human secondary antibody (anti-human Ig whole antibody from sheep (Amersham Life Science, NA933)) diluted 1:100 in dilution buffer was added to the wells and incubated for 1 hour at 37°C. The plates were washed and OPD (o-phenylenediamine dihydrochloride) substrate with H₂O₂ in substrate buffer (50mM phosphate/25mM citrate, pH 7.2) was added to the wells. For a kinetics ELISA, the plate was read repeatedly (2 minute intervals for 15 minutes) unstopped (without "stop" buffer). Plates were read at 450nm.

Results

The results of the above experiment are presented in Table 8 and in Figure 5. The animals of group 2 received intranodal injections of ALVAC(2)-gp100(mod) followed by boosts with the modified gp100 peptides 209(2M) and 290(9V); the animals in group 3 received a subcutaneous

injection of the ALVAC(2) construct followed by peptide boosts; the animals in group 1 received intranodal injections of saline as a control.

As can be seen from Figure 5, intranodal injection of the antigens induced a humoral response that was much greater than when the antigen
5 was injected subcutaneously.

In summary, the results of this Example demonstrate that intranodal injection of a tumor antigen induces both a humoral and cell mediated response that is much greater than when the tumor antigen is injected by the conventional subcutaneous route of administration.

10 While the present invention has been described with reference to what are presently considered to be the preferred examples, it is to be understood that the invention is not limited to the disclosed examples. To the contrary, the invention is intended to cover various modifications and equivalent arrangements included within the spirit and scope of the
15 appended claims.

All publications, patents and patent applications are herein incorporated by reference in their entirety to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference in its entirety.

TABLE 1

Group Number	Route of administration	Treatment days and compound administered	Number of Animals
1	Intranodal	Saline (NaCl 0.9%): days 28, 42, 56 Then 70, 71, 72, 73, 74 Then 84, 85, 86, 87 and 88	4
2	Intranodal	ALVAC(2) - gp100 mod: days 28, 42, 56 *mgp100 peptides: days 70, 71, 72, 73, 74 Then 84, 85, 86, 87 and 88	4
3	Subcutaneous	Saline (NaCl 0.9%): day 1 ALVAC(2) - gp100 mod: days 28, 42, 56 *mgp100 peptides: days 70 and 84	4

*209(2M)-IMDQVPFSY; 290(9V) YLEPGPVTV

- 5
- Group 1 animals (control) received the control article (saline for injection (NaCl 0.9%)).
 - Group 3 animals received the control article (saline for injection (NaCl 0.9%)) on day 1 only.

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TABLE 2

Group Number	Dose level	Dose volume (ml/administration)
1	Saline (NaCl 0.9%): 0	0.250
2	Dose: $0.25 \times 10^{7.4}$ CCID 50 ALVAC (2) - gp100 mod: $0.25 \times 10^{7.4}$ CCID50	0.250
	Dose: 200 μ g (Total) of peptides IMDQVPFSY (209(2M)), and YLEPGPVTV (290(9V)) (100 μ g each)	0.2
3	Saline (NaCl 0.9%)	0.250
	ALVAC(2) - gp100 mod: $0.25 \times 10^{7.4}$ CCID 50	0.250
	Dose: 200 μ g (Total) of peptides IMDQVPFSY (209(2M)), and YLEPGPVTV (290(9V)) (100 μ g each)	0.2

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TABLE 3

Days	Sites used
1 and 28	lower left
42	upper left
56	upper right
70	lower left
84	lower right

TABLE 4

Peptide Pool #1

Peptide	Sequence	SEQ.ID.NO.
1329	HLAVIGALLAVGAIK	SEQ.ID.NO.3
1330	GALLAVGATKVPRNQ	SEQ.ID.NO.4
1331	VGATKVPRNQDWLGV	SEQ.ID.NO.5
1332	VPRNQDWLGVSRLR	SEQ.ID.NO.6
1333	DWLGVSRLRRTKAWN	SEQ.ID.NO.7
1334	SRQLRRTKAWNROLYP	SEQ.ID.NO.8
1335	TKAWNROLYPEWTEA	SEQ.ID.NO.9
1336	ROLYPEWTEAORLDC	SEQ.ID.NO.10
1337	EWTEAORLDCWRGGQ	SEQ.ID.NO.11
1338	ORLDCWRGGQVSLKV	SEQ.ID.NO.12
1339	WRGGQVSLKVSNDGP	SEQ.ID.NO.13
1340	VSLKVSNDGPTLIGA	SEQ.ID.NO.14
1344	IALNFPQSQKVLDPG	SEQ.ID.NO.15
1345	PGSQKVLDPGQVIWV	SEQ.ID.NO.16
1346	VLPDGQVIWVNNTII	SEQ.ID.NO.17
1347	QVIWVNNTIINGSQV	SEQ.ID.NO.18
1348	NNTIINGSQVWGGQP	SEQ.ID.NO.19
1349	NGSQVWGGQPVYPQE	SEQ.ID.NO.20
1350	WGGQPVYPQETDDAC	SEQ.ID.NO.21
1351	VYPQETDDACIFPDG	SEQ.ID.NO.22
1352	TDDACIFPDGGPCPS	SEQ.ID.NO.23
1353	IFPDGGPCPSGSWSQ	SEQ.ID.NO.24
1355	GSWSQKRSEVYVWKT	SEQ.ID.NO.25
1356	KRSFVYVWKTWGQYW	SEQ.ID.NO.26
1357	YVWKTWGQYWQVLGG	SEQ.ID.NO.27
1358	WGQYWQVLGGPVSL	SEQ.ID.NO.28
1359	QVLGGPVSLSIGTG	SEQ.ID.NO.29

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TABLE 5

Peptide Pool #2

Peptide	Sequence	SEQ.ID.NO.
1360	PVSGLSIGTGRAMLG	SEQ.ID.NO.30
1361	SIGTGRAMLGHTME	SEQ.ID.NO.31
1362	RAMLGHTMEVTVYH	SEQ.ID.NO.32
1363	THTMEVTVYHRRGSR	SEQ.ID.NO.33
1364	VTVYHRRGSRSYVPL	SEQ.ID.NO.34
1365	RRGSRSYVPLAHSSS	SEQ.ID.NO.35
1366	SYVPLAHSSSAFTIT	SEQ.ID.NO.36
1368	AFTITDQVPFSVSVS	SEQ.ID.NO.37
1369	DQVPFSVSVSQLRAL	SEQ.ID.NO.38
1370	SVSVSQLRALDGGNK	SEQ.ID.NO.39
1372	DGGNKHFLRNQPLTF	SEQ.ID.NO.40
1373	HFLRNQPLTFALQLH	SEQ.ID.NO.41
1374	QPLTFALQLHDPGY	SEQ.ID.NO.42
1375	ALQLHDPGYLAED	SEQ.ID.NO.43
1379	DFGDSSGTLISRALV	SEQ.ID.NO.44
1380	STGLISRALVVHTY	SEQ.ID.NO.45
1381	SRALVVHTYLEPGP	SEQ.ID.NO.46
1382	VHTYLEPGPVTAQV	SEQ.ID.NO.47
1383	LEPGPVTAQVVLQAA	SEQ.ID.NO.48
1384	VTAQVVLQAAIPLTS	SEQ.ID.NO.49
1385	VLQAAIPLTSCGSSP	SEQ.ID.NO.50
1386	IPLTSCGSSPVPGETT	SEQ.ID.NO.51
1388	VPGETTDGHRPTAEAP	SEQ.ID.NO.52
1389	DGHRPTAEAPNTTAG	SEQ.ID.NO.53
1390	TAEAPNTTAGQVPTT	SEQ.ID.NO.54
1392	QVPTTEVVGTTPGQA	SEQ.ID.NO.55
1393	EVVGTTTPGOAPTAEP	SEQ.ID.NO.56

40
TABLE 6

Peptide Pool #3

Peptide	Sequence	SEQ.ID.NO.
1394	TPGOAPTAEPSGTTS	SEQ.ID.NO.57
1395	PTAEPSGTTSVQVPT	SEQ.ID.NO.58
1396	SGTTSVQVPTTEVIS	SEQ.ID.NO.59
1397	VQVPTTEVISTAPVQ	SEQ.ID.NO.60
1398	TEVISTAPVQMPAE	SEQ.ID.NO.61
1399	TAPVQMPAEESTGMT	SEQ.ID.NO.62
1400	MPTAEESTGMTPEKVP	SEQ.ID.NO.63
1401	STGMTPEKVPVSEVM	SEQ.ID.NO.64
1402	PEKVPVSEVMGTTLA	SEQ.ID.NO.65
1403	VSEVMGTTLAEMSTP	SEQ.ID.NO.66
1404	GTTLAEMSTPEATGM	SEQ.ID.NO.67
1405	EMSTPEATGMTPAEV	SEQ.ID.NO.68
1408	SIVVLSGTTAAQVTT	SEQ.ID.NO.69
1409	SGTTAAQVTTTEWVE	SEQ.ID.NO.70
1410	AQVTTTEWVETTARE	SEQ.ID.NO.71
1411	TEWVETTARELPIPE	SEQ.ID.NO.72
1412	TTARELPIPEPEGPD	SEQ.ID.NO.73
1413	LPIPEPEGPDASSIM	SEQ.ID.NO.74
1414	PEGPDASSIMSTESI	SEQ.ID.NO.75
1415	ASSIMSTESITGSLG	SEQ.ID.NO.76
1416	STESITGSLGPLLDG	SEQ.ID.NO.77
1417	TGSLGPLLDGTATLR	SEQ.ID.NO.78
1418	PLLDGTATLRLVKRQ	SEQ.ID.NO.79
1419	TATLRLVKRQVPLDC	SEQ.ID.NO.80
1420	LVKRQVPLDCVLYRY	SEQ.ID.NO.81
1421	VPLDCVLYRYGSFSV	SEQ.ID.NO.82
1422	VLYRYGSFSVTLDIV	SEQ.ID.NO.83

Table 7

Peptide Pool #4

Peptide	Sequence	SEQ.ID.NO.
1424	TLDIVOGIESAEILQ	SEQ.ID.NO.84
1425	QGIESAEILQAVPSG	SEQ.ID.NO.85
1426	AEILQAVPSGEGDAF	SEQ.ID.NO.86
1427	AVPSGEGDAFELTVS	SEQ.ID.NO.87
1428	EGDAFELTVSCQGGL	SEQ.ID.NO.88
1429	ELTVSCQGGLPKEAC	SEQ.ID.NO.89
1430	COGGLPKEACMEISS	SEQ.ID.NO.90
1431	PKEACMEISSPGCQP	SEQ.ID.NO.91
1432	MEISSPGCQPPAQR	SEQ.ID.NO.92
1434	PAQRLCOPVLPSPAC	SEQ.ID.NO.93
1435	COPVLPSPACQLVLH	SEQ.ID.NO.94
1436	PSPACQLVLHQILKG	SEQ.ID.NO.95
1437	QLVLHQILKGGSGTY	SEQ.ID.NO.96
1441	LADTNSLAVVSTQLI	SEQ.ID.NO.97
1442	SLAVVSTQLIMPGQE	SEQ.ID.NO.98
1443	STQLIMPGQEAGLGQ	SEQ.ID.NO.99
1444	MPGQEAGLGQVPLIV	SEQ.ID.NO.100
1445	AGLGQVPLIVGILLV	SEQ.ID.NO.101
1448	LMAVVLASLIYRRRL	SEQ.ID.NO.102
1450	YRRRLMKQDFSVPL	SEQ.ID.NO.103
1451	MKQDFSVPLPHSSS	SEQ.ID.NO.104
1452	SVPLPHSSSHWLRL	SEQ.ID.NO.105
1453	PHSSSHWLRLPRIFC	SEQ.ID.NO.106
1454	HWLRLPRIFCSCPIG	SEQ.ID.NO.107
1455	PRIFCSCPIGENSPL	SEQ.ID.NO.108

TABLE 8

Monkey #	DAY (mOD/min)			
	0	57	68	96
1	3	5	2	2
2	4	6	12	10
3	7	6	10	8
4	7	6	8	8
5	5	9	20	15
6	11	8	10	12
7	11	23	51	30
8	7	30	70	22
9	1	7	5	3
10	2	6	6	4
11	3	7	14	8
12	6	9	15	6

We claim:

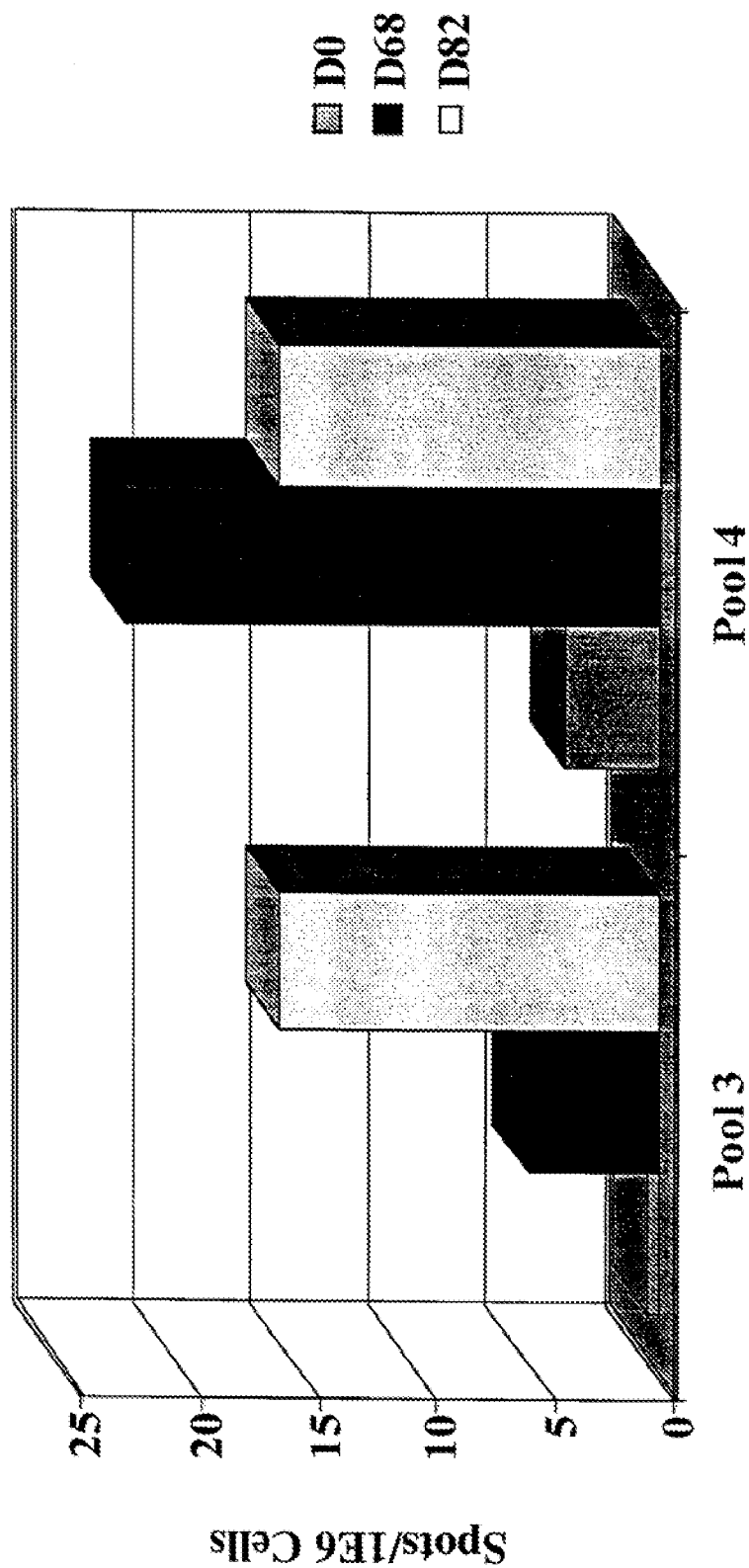
1. A method for inducing an immune response in an animal to a tumor
5 antigen comprising administering an effective amount of a tumor
antigen or a nucleic acid sequence encoding a tumor antigen to a
lymphatic site in the animal.
2. A method according to claim 1 wherein the tumor antigen is selected
10 from the group consisting of CEA, gp100, the MAGE family of proteins,
DAGE, GAGE, RAGE, NY-ESO 1, Melan-A/MART 1, TRP-1, TRP-2,
tyrosinase, HER-2/neu, MUC-1, p53, KSA, PSA, PSMA, and fragments
and modified versions thereof.
- 15 3. A method according to claim 1 or 2 wherein the lymphatic site is a
lymph node.
4. A method according to any one of claims 1 to 3 wherein the nucleic
acid is selected from the group consisting of viral nucleic acid,
20 bacterial DNA, plasmid DNA, naked/free DNA, and RNA.
5. A method according to claim 4 wherein the viral nucleic acid is
selected from the group consisting of adenoviral, alphaviral and
poxviral nucleic acid.
25
6. A method according to claim 5 wherein the poxviral nucleic acid is
selected from the group consisting of avipox, orthopox and suipox
nucleic acid.
- 30 7. A method according to claim 5 wherein the poxviral nucleic acid is
selected from the group consisting of vaccinia, fowl pox, canarypox
and swinepox nucleic acid.

8. A method according to claim 5 wherein the poxviral nucleic acid is selected from the group consisting of MVA, NYVAC, TROVAC, and ALVAC nucleic acid.
- 5 9. A method according to any one of claims 1 to 8 wherein the nucleic acid is contained in a vector.
- 10 10. A method according to claim 9 wherein the vector is a recombinant virus or bacteria.
11. A method according to claim 10 wherein the recombinant virus is selected from the group consisting of adenovirus, alphavirus and poxvirus.
- 15 12. A method according to claim 11 wherein the poxvirus is selected from the group consisting of avipox, orthopox and suipox.
- 20 13. A method according to claim 11 wherein the poxvirus is selected from the group consisting of vaccinia, fowlpox, canarypox and swinepox.
14. A method according to claim 11 wherein the poxvirus is selected from the group consisting of MVA, NYVAC, TROVAC, and ALVAC.
- 25 15. A method according to any one of claims 1 to 8 wherein the nucleic acid is contained in a cell.
16. A method according to any one of claims 1 to 14 wherein the tumor antigen or nucleic acid coding therefor is contained in a vaccine.

- 45
17. A method according to any one of claims 1 to 16 wherein the tumor antigen is gp100, CEA or a fragment or modified version of gp100 or CEA.
- 5 18. A method according to claim 17 wherein the modified gp100 comprises the sequence IMDQVPFSY (SEQ ID NO: 1) and/or YLEPGPVTV (SEQ ID NO:2).
- 10 19. A method according to claim 17 wherein the modified CEA comprises the sequence shown in Figure 8 (SEQ ID NO:112) and/or YLSGADLNL (SEQ ID NO:113).

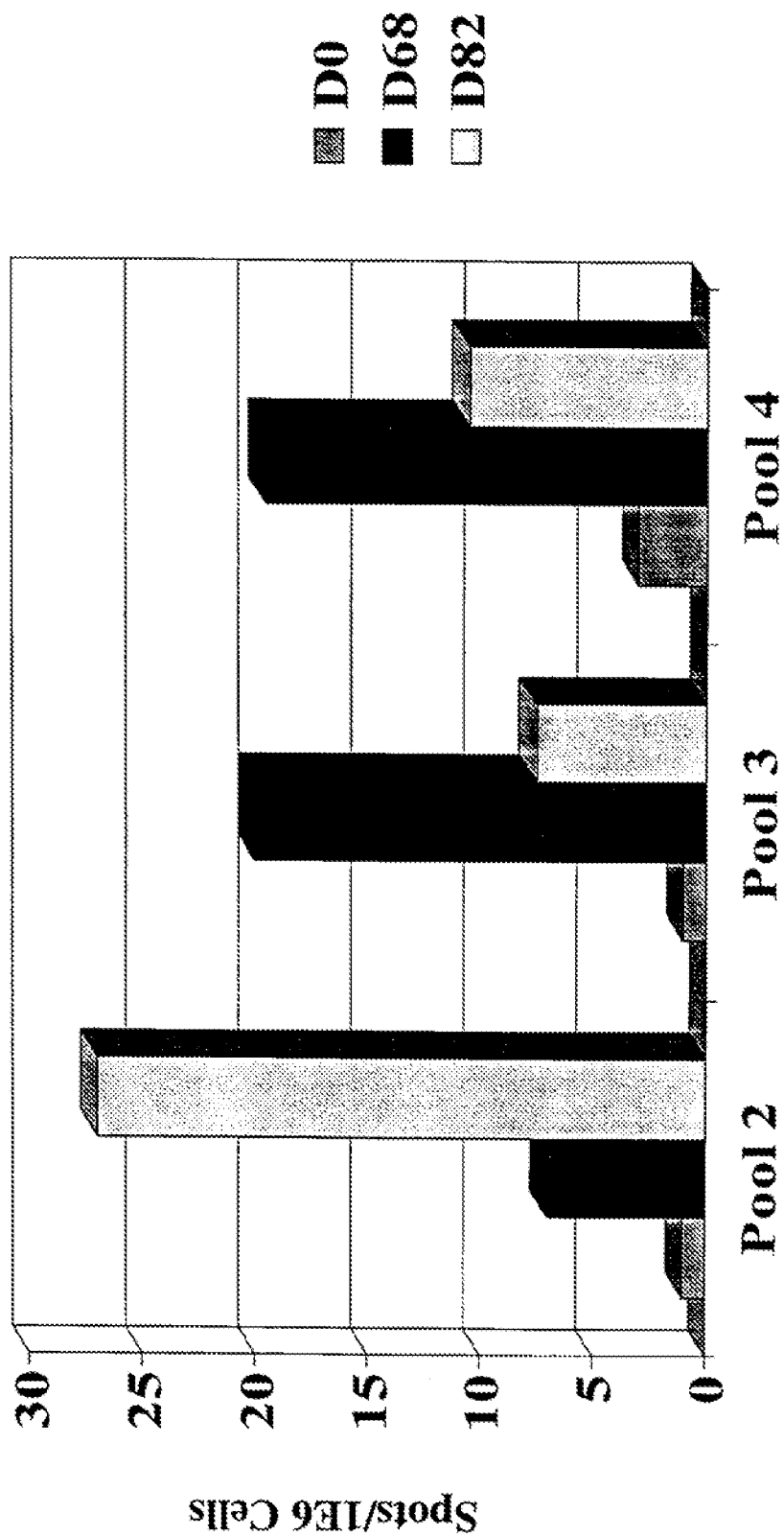
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FIGURE 1
Monkey #6 (Intranodal Administration)



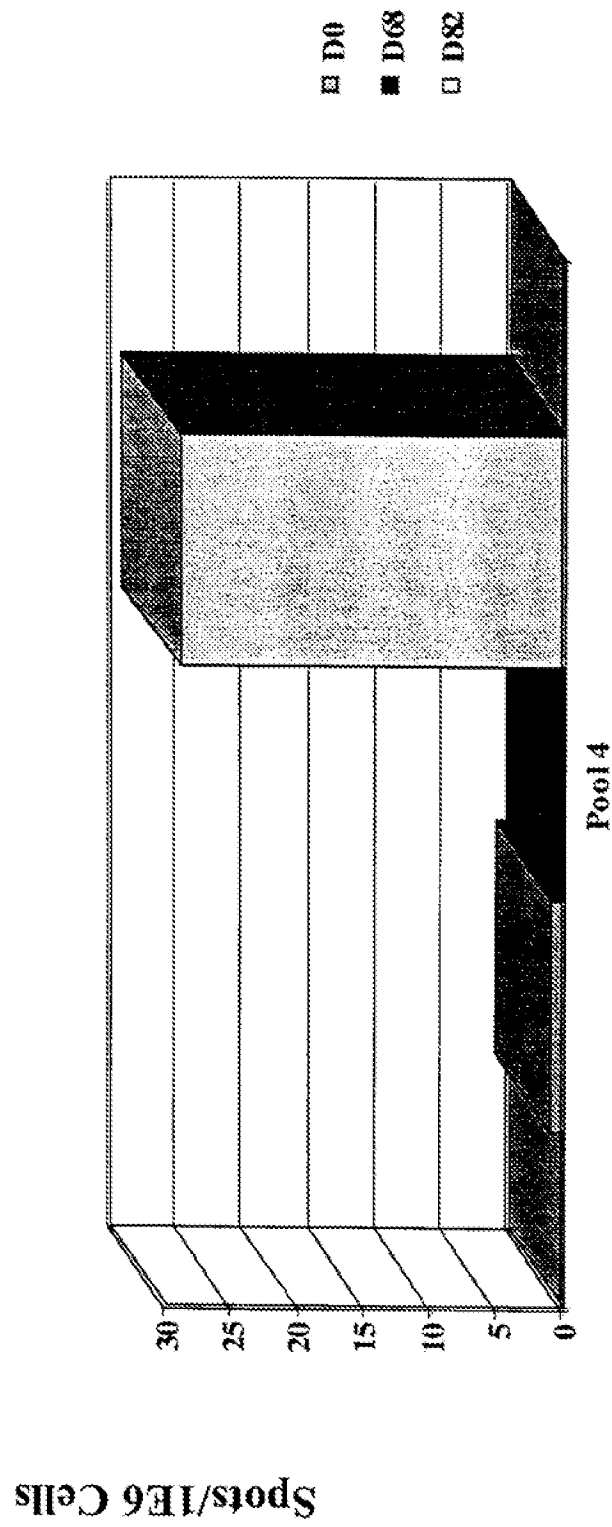
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FIGURE 2
Monkey #7 (Intranodal Administration)



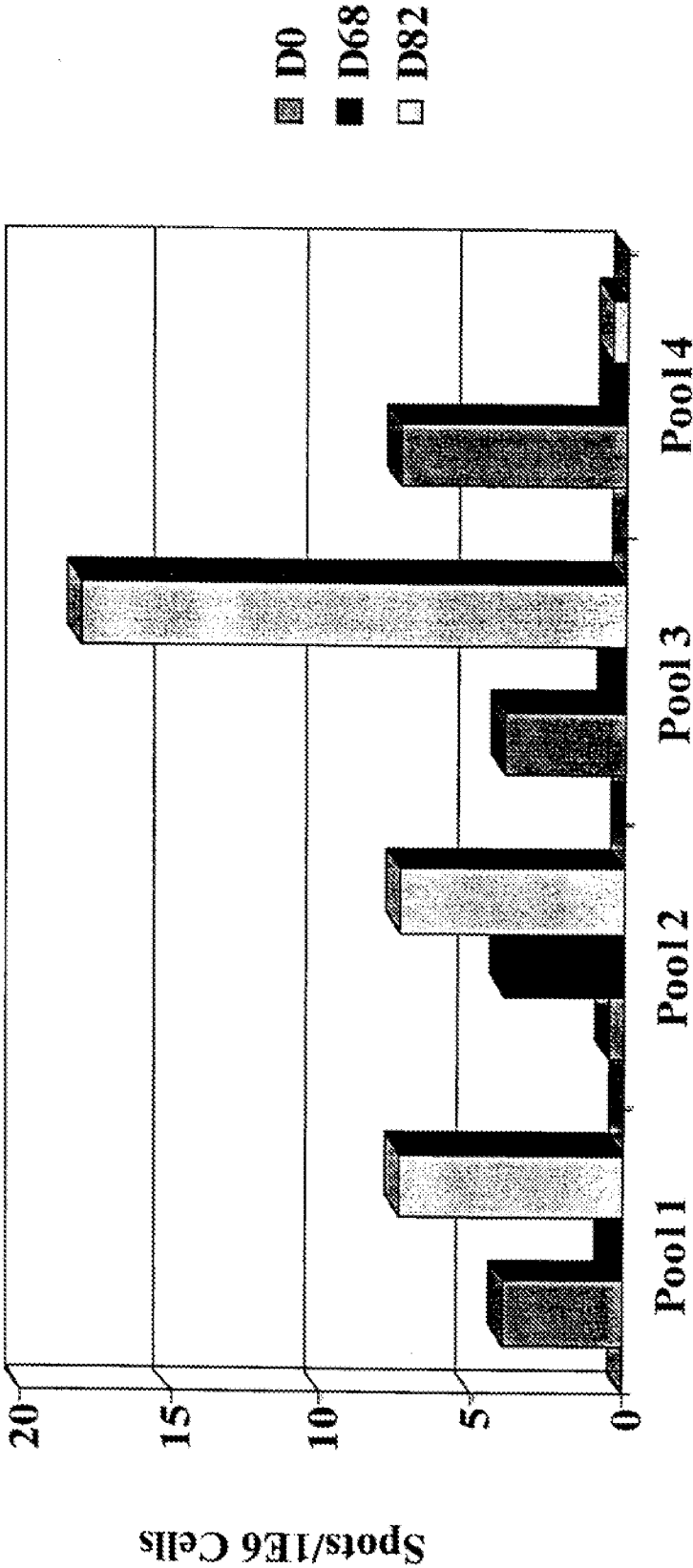
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FIGURE 3
Monkey # 11 (Subcutaneous Administration)



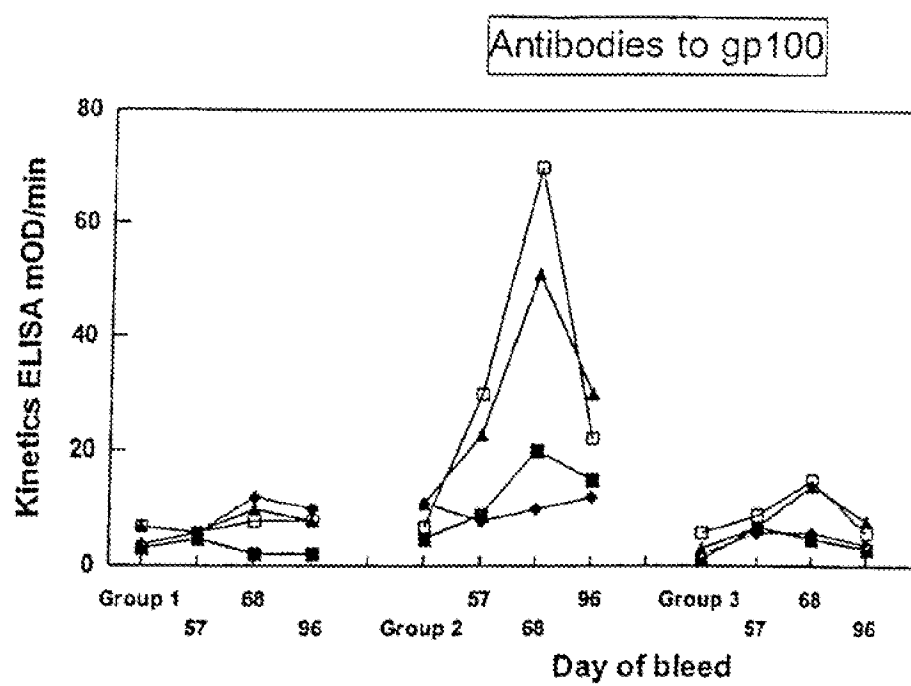
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FIGURE 4
Monkey #10 (Subcutaneous Administration)



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FIGURE 5



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FIGURE 6

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          ATGG ATCTGGTGCT AAAAAAGATGC CTTCTTCATT TGGCTGTGAT
AGGTGCTTTG CTGGCTGTGG GGGCTACAAA AGTACCCAGA AACCAGGACT GGCTTGGTGT
CTCAAGGCAA CTCAGAACCA AAGCCTGGAA CAGGCAGCTG TATCCAGAGT GGACAGAAGC
CCAGAGACTT GACTGCTGGA GAGGTGGTCA AGTGTCCCTC AAGGTCAGTA ATGATGGGCC
TACACTGATT GGTGCAAATG CCTCCTTCTC TATTGCCCTG AACTTCCCTG GAAGCCAAAA
GGTATTGCCA GATGGGCAGG TTATCTGGGT CAACAATACC ATCATCAATG GGAGCCAGGT
GTGGGGAGGA CAGCCAGTGT ATCCCCAGGA AACTGACGAT GCCTGCATCT TCCCCTGATGG
TGGACCTTGC CCATCTGGCT CTTGGTCTCA GAAGAGAAGC TTTGTTTATG TCTGGAAGAC
CTGGGGCCAA TACTGGCAAG TTCTAGGGGG CCCAGTGTCT GGGCTGAGCA TTGGGACAGG
CAGGGCAATG CTGGGCACAC ACACGATGGA AGTGACTGTC TACCATCGCC GGGGATCCCG
GAGCTATGTG CCTCTTGCTC ATTCCAGCTC AGCCTTCACC ATTATGGACC AGGTGCCTTT
CTCCGTGAGC GTGTCCCAGT TCGGGGCCCT GGATGGAGGG AACAAAGCACT TCCTGAGAAA
TCAGCCTCTG ACCTTTGCCC TCCAGCTCCA TGACCCCACT GGCTATCTGG CTGAAGCTGA
CCTCTCCTAC ACCTGGGACT TTGGAGACAG TAGTGGAAACC CTGATCTCTC GGGCCTTGT
GGTCACTCAT ACTTACCTGG AGCCTGGCCC AGTCACTGTT CAGGTGGTCC TGCAGGCTGC
CATTCCTCTC ACCTCCTGTG GCTCCTCCCC AGTTCCAGGC ACCACAGATG GGCACAGGCC
AACTGCAGAG GCCCCTAACA CCACAGCTGG CCAAGTGCTT ACTACAGAAG TTGTGGGTAC
TACACCTGGT CAGGCGCCAA CTGCAGAGCC CTCTGGAACC ACATCTGTGC AGGTGCCAAC
CACTGAAGTC ATAAGCACTG CACCTGTGCA GATGCCAACT GCAGAGAGCA CAGGTATGAC
ACCTGAGAAG GTGCCAGTTT CAGAGGTCAT GGGTACCACA CTGGCAGAGA TGTCAACTCC
AGAGGCTACA GGTATGACAC CTGCAGAGGT ATCAATTGTG GTGCTTTCTG GAACCACAGC
TGCACAGGTA ACAACTACAG AGTGGGTGGA GAUCCACAGCT AGAGAGCTAC CTATCCCTGA
GCCTGAAGGT CCAGATGCCA GCTCAATCAT GTCTACGGAA AGTATTACAG GTTCCCCTGG
CCCCCTGCTG GATGGTACAG CCACCTTAAG GCTGGTGAAG AGACAAGTCC CCCTGGATTG
TGCCGAGATC CTGCAGGCTG TGCCGTCCGG TGAGGGGGAT GCATTTGAGC TGA CTGTGTC
CTGCCAAGGC GGGCTGCCCC AGGAAGCCTG CATGGAGATC TCATCGCCAG GGTGCCAGCC
CCCTGCCCCAG CGGCTGTGCC AGCCTGTGCT ACCCAGCCCC GCCTGCCAGC TGGTCTGCA
CCAGATACTG AAGGCTGGCT CGGGGACATA CTGCCTCAAT GTGTCTCTGG CTGATACCAA
CAGCCTGGCA GTGGTCAQCA CCCAGCTTAT CATGCCTGGT CAAGAAGCAG GCCTTGGGCA
GGTTCCGCTG ATCGTGGGCA TCTTGCTGGT GTTGATGGCT GTGGTCCTTG CATCTCTGAT
ATATAGGCGC AGACTTATGA AGCAAGACTT CTCCGTACCC CAGTTGCCAC ATAGCAGCAG
TCACTGGCTG CGTCTACCCC GCATCTTCTG CTCTTGTCCT ATTGGTGAGA ACAGCCCCCT
CCTCAGTGGG CAGCAGGTCT GA

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FIGURE 7

Met	Asp	Leu	Val	Leu	Lys	Arg	Cys	Leu	Leu	His	Leu	Ala	Val	Ile	Gly	1	5	10	15
Ala	Leu	Leu	Ala	Val	Gly	Ala	Thr	Lys	Val	Pro	Arg	Asn	Gln	Asp	Trp	20	25	30	
Leu	Gly	Val	Ser	Arg	Gln	Leu	Arg	Thr	Lys	Ala	Trp	Asn	Arg	Gln	Leu	35	40	45	
Tyr	Pro	Glu	Trp	Thr	Glu	Ala	Gln	Arg	Leu	Asp	Cys	Trp	Arg	Gly	Gly	50	55	60	
Gln	Val	Ser	Leu	Lys	Val	Ser	Asn	Asp	Gly	Pro	Thr	Leu	Ile	Gly	Ala	65	70	75	80
Asn	Ala	Ser	Phe	Ser	Ile	Ala	Leu	Asn	Phe	Pro	Gly	Ser	Gln	Lys	Val	85	90	95	
Leu	Pro	Asp	Gly	Gln	Val	Ile	Trp	Val	Asn	Asn	Thr	Ile	Ile	Asn	Gly	100	105	110	
Ser	Gln	Val	Trp	Gly	Gly	Gln	Pro	Val	Tyr	Pro	Gln	Glu	Thr	Asp	Asp	115	120	125	
Ala	Cys	Ile	Phe	Pro	Asp	Gly	Gly	Pro	Cys	Pro	Ser	Gly	Ser	Trp	Ser	130	135	140	
Gln	Lys	Arg	Ser	Phe	Val	Tyr	Val	Trp	Lys	Thr	Trp	Gly	Gln	Tyr	Trp	145	150	155	160
Gln	Val	Leu	Gly	Gly	Pro	Val	Ser	Gly	Leu	Ser	Ile	Gly	Thr	Gly	Arg	165	170	175	
Ala	Met	Leu	Gly	Thr	His	Thr	Met	Glu	Val	Thr	Val	Tyr	His	Arg	Arg	180	185	190	
Gly	Ser	Arg	Ser	Tyr	Val	Pro	Leu	Ala	His	Ser	Ser	Ser	Ala	Phe	Thr	195	200	205	
Ile	Met	Asp	Gln	Val	Pro	Phe	Ser	Val	Ser	Val	Ser	Gln	Leu	Arg	Ala	210	215	220	
Leu	Asp	Gly	Gly	Asn	Lys	His	Phe	Leu	Arg	Asn	Gln	Pro	Leu	Thr	Phe	225	230	235	240
Ala	Leu	Gln	Leu	His	Asp	Pro	Ser	Gly	Tyr	Leu	Ala	Glu	Ala	Asp	Leu	245	250	255	
Ser	Tyr	Thr	Trp	Asp	Phe	Gly	Asp	Ser	Ser	Gly	Thr	Leu	Ile	Ser	Arg	260	265	270	
Ala	Leu	Val	Val	Thr	His	Thr	Tyr	Leu	Glu	Pro	Gly	Pro	Val	Thr	Val	275	280	285	
Gln	Val	Val	Leu	Gln	Ala	Ala	Ile	Pro	Leu	Thr	Ser	Cys	Gly	Ser	Ser	290	295	300	
Pro	Val	Pro	Gly	Thr	Thr	Asp	Gly	His	Arg	Pro	Thr	Ala	Glu	Ala	Pro	305	310	315	320
Asn	Thr	Thr	Ala	Gly	Gln	Val	Pro	Thr	Thr	Glu	Val	Val	Gly	Thr	Thr	325	330	335	
Pro	Gly	Gln	Ala	Pro	Thr	Ala	Glu	Pro	Ser	Gly	Thr	Thr	Ser	Val	Gln	340	345	350	
Val	Pro	Thr	Thr	Glu	Val	Ile	Ser	Thr	Ala	Pro	Val	Gln	Met	Pro	Thr	355	360	365	

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FIGURE 7 (CONT'D)

Ala	Glu	Ser	Thr	Gly	Met	Thr	Pro	Glu	Lys	Val	Pro	Val	Ser	Glu	Val
370						375					380				
Met	Gly	Thr	Thr	Leu	Ala	Glu	Met	Ser	Thr	Pro	Glu	Ala	Thr	Gly	Met
385					390					395					400
Thr	Pro	Ala	Glu	Val	Ser	Ile	Val	Val	Leu	Ser	Gly	Thr	Thr	Ala	Ala
				405					410					415	
Gln	Val	Thr	Thr	Thr	Glu	Trp	Val	Glu	Thr	Thr	Ala	Arg	Glu	Leu	Pro
			420					425					430		
Ile	Pro	Glu	Pro	Glu	Gly	Pro	Asp	Ala	Ser	Ser	Ile	Met	Ser	Thr	Glu
			435				440					445			
Ser	Ile	Thr	Gly	Ser	Leu	Gly	Pro	Leu	Leu	Asp	Gly	Thr	Ala	Thr	Leu
450						455					460				
Arg	Leu	Val	Lys	Arg	Gln	Val	Pro	Leu	Asp	Cys	Val	Leu	Tyr	Arg	Tyr
465					470					475					480
Gly	Ser	Phe	Ser	Val	Thr	Leu	Asp	Ile	Val	Gln	Gly	Ile	Glu	Ser	Ala
				485					490					495	
Glu	Ile	Leu	Gln	Ala	Val	Pro	Ser	Gly	Glu	Gly	Asp	Ala	Phe	Glu	Leu
			500					505					510		
Thr	Val	Ser	Cys	Gln	Gly	Gly	Leu	Pro	Lys	Glu	Ala	Cys	Met	Glu	Ile
		515					520					525			
Ser	Ser	Pro	Gly	Cys	Gln	Pro	Pro	Ala	Gln	Arg	Leu	Cys	Gln	Pro	Val
530						535					540				
Leu	Pro	Ser	Pro	Ala	Cys	Gln	Leu	Val	Leu	His	Gln	Ile	Leu	Lys	Gly
545					550					555					560
Gly	Ser	Gly	Thr	Tyr	Cys	Leu	Asn	Val	Ser	Leu	Ala	Asp	Thr	Asn	Ser
				565					570					575	
Leu	Ala	Val	Val	Ser	Thr	Gln	Leu	Ile	Met	Pro	Gly	Gln	Glu	Ala	Gly
			580					585					590		
Leu	Gly	Gln	Val	Pro	Leu	Ile	Val	Gly	Ile	Leu	Leu	Val	Leu	Met	Ala
		595					600					605			
Val	Val	Leu	Ala	Ser	Leu	Ile	Tyr	Arg	Arg	Arg	Leu	Met	Lys	Gln	Asp
610						615					620				
Phe	Ser	Val	Pro	Gln	Leu	Pro	His	Ser	Ser	Ser	His	Trp	Leu	Arg	Leu
625					630					635					640
Pro	Arg	Ile	Phe	Cys	Ser	Cys	Pro	Ile	Gly	Glu	Asn	Ser	Pro	Leu	Leu
				645					650					655	
Ser	Gly	Gln	Gln	Val											
			660												

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FIGURE 8

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ATGGAGTCTCCCTCGGCCCTCCCCACASATGGTGCATCCCCTGGCAGAGGCTCCTGCTC
1  -----+----- 60
TACCTCAGAGGAGCCGCGGAGGGGTGTCTACCACGTAGGGGACCGTCTCCGAGGACGAG
a  M E S P S A P P H R W C I P W Q R L L L -
ACAGCCTCACTTCTAACCTTCTGGAACCCGCCCCACCACTGCCAAGCTCACTATTGAATCC
61  -----+----- 120
TGTGCGAGTGAAGATTGGAAGACCTTGGGCGGCTGGTGACGGTTGGAGTGATAACTTAGG
a  T A S L L T F W N P P T T A K L T I E S -
ACGCCGTTCAATGTCGAGAGGGGAAGGAGGTCTTCTACTTGTCCACAATCTGCCCCAG
121  -----+----- 180
TGGGCAAGTTACAGGGTCTCCCTTCTCCAGGAAGATGAACAGGTGTTAGACGGGGTC
a  T P F N V A E G K E V L L L V H N L P Q -
CATCTTTTGGCTACAGCTGGYACAAAGGTGAAAGAGTGGATGGCAACCGTCAAATTATA
181  -----+----- 240
GTAGAAAAACCGATGTCGACCATGTTTCCACTTCTCACCTACCGTTGGCAGTTTAATAT
a  H L F G Y S W Y K G E R V D G N R Q I I -
GGATATGTAATAGGAACFCAACAGCTACCCAGSGCCCGCATACAGTGGTCCGAGAGATA
241  -----+----- 300
CCTATACATTATCCTTGAGTTGTTCCGATGGGGTCCCGGGCGTATGTCACCAAGCTCTCTAT
a  G Y V I G T Q Q A T P G P A Y S G R E I -
ATATACCCCAATGCATCCCTGCTGATCCAGAACATCATCCAGAATGACACAGGATTCTAC
301  -----+----- 360
TNTATGGGGTTACGTAGGGACGACTAGGTCTTGTAGTAGGTCTTACTGTGTDCTAAGATG
a  I Y P N A S L L I Q N I I Q N D T G F Y -
ACCCACACGTCATAAAGTCAGATCTTGTGAATGAAGAAGCAACTGGCCAGTCCGGGTA
361  -----+----- 420
TGGGATGTGCAGTATTTAGTCTAGAACACTTACTTCTTGGTTGACCGGTCAAGGCCCAT
a  T L H V I K S D L V N E E A T G Q F R V -
TACCCGGAGCTGCCAAGCCCTCCATCTCCAGCAACCACTCCAAACCGTGGAGGACAAG
421  -----+----- 480
ATGGGCCCTCGACGGGTTCCGGAGGTAGAGGTGTTGTTGAGGTTTGGGCACCTCCTGTT
a  Y P E L P K P S I S S N N S K P V E D K -
GATGCTGTGGCCTTCACTGTGAACCTGAGACTCAGGACGCAACCTACCTGTGTGGGTA
481  -----+----- 540
CTACGACACCGGAAGTGGACACTTGGACTCTGAGTCTGCGTTGGATGGACACCACCCAT
a  D A V A F T C E P E T Q D A T Y L W W V -
AACAATCAGAGCCTCCCGGTCACTCCAGGCTGCAGCTGTCCAATGGCAACAGGACCCCTC
541  -----+----- 600
TTGTTAGTCTCGAGGGGCCAGTCAGGGTCCGACGTCGACAGGTTACCGTTGTCCTGGGAG
a  N N Q S L P V S P R L Q L S N G N R T L -
ACTCTATTCAATGTCACAAGAAATGACACAGCAAGCTACAAATGTGAAGGCCAGAACCCA
601  -----+----- 660
TGAGATAAGTTACACTCTTCTTTACTGTGTCGTTCCGATGTTTACACTTGGGTCTTGGGT
a  T L F N V T R N D T A S Y K C E T Q N P -
GTGAGTGGCAGCCCACTGATTCACTCATCCTGAATGTCTCTATGGGCCGAGTGGCCCC
661  -----+----- 720
CACTCACGCTCCGCGTCACTAAGTCAGTAGGACTTACAGAGATACCGGGCTACGGGGG
a  V S A R R S D S V I L N V L Y G P D A F -

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FIGURE 8 (CONT'D)

ACCATTTCCTCTTAACACATCTTACAGATCAGGGGAAATCTGAACCTCTCTGCCAC
721 -----+----- 780
TGSTAAAGGGGAGATTTGTGTAGAATGTCTAGTCCCCCTTTAGACTTGGAGAGGACCGTG
a T I S P L N T S Y R S G E N L N L S C H -
GCAGCCTCTAACCACCTGCACAGTACTCTTGGTTTGTCAATGGGACTTTCCAGCAATCC
781 -----+----- 840
CGTCGGAGATTGGGTGGACGTGTCATGAGAACCAACAGTTACCCCTGAAGGTGCTTAGG
a A A S N P P A Q Y S W F V N G T F Q Q S -
ACCCAAGAGCTCTTTATCCCCAACATCACTGTGAATAATAGTGGATCCTATACGTGCCAA
841 -----+----- 900
TGGGTTCTCGAGAAATAGGGCTTGTACTGACACTTATTATCACCTAGGATATGCACGGTT
a T Q E L F I P N I T V N N S S S Y T C Q -
GCCCATAACTCAGACACTGGCCTCAATAGGACCAAGTCCAGACGATCAGAGTCTATGAG
901 -----+----- 960
CGGTATTGAGTCTGTGACCGGAGTTATCTGTGTGTCAGTGTCTAGTGTGAGATACTC
a A H N S D T G L N R T T V T T I T V Y E -
CCACCCAACCCCTTCATCACCAGCAACAACCTCCACCCCGTGGAGGATGAGGATGCTGTA
961 -----+----- 1020
GGTGGGTTTGGGAAGTAGTGGTCTGTGTGAGGTTGGGGCACCTCCTACTCCTACGACAT
a P P K P F I T S N N S N P V E D E D A V -
GCCTTAACCTGTGAACCTGAGATTGAGAACACACCTACCTGTGGTGGTAAATTAATCAG
1021 -----+----- 1080
CGGAATTGGACACTTGGACTCTAAGTCTTGTGTGAGTGGACACCCACCTATTATTAGTC
a A L T C E F E I Q N T T Y L W N V N N Q -
AGCCTCCCGSTCAGTCCCAGGCTGCAGGTGTCCAATGACAACAGGACCCCTCACTCTACTC
1081 -----+----- 1140
TCGGAGGGCCAGTCAGGCTCCGACGTCGACAGGTTACTGTTGCTGGGAGTGGATGAG
a S L P V S P R L Q L S N D N R T L T L L -
AGTGTCAACAGGAATGATGTAGGACCCCTATGAGTGTGGAATCCAGAACGAATTAAGTGT
1141 -----+----- 1200
TCACAGTGTTCCTTACTACATCCTGGGATACTCACACCTTAGGTCTTGCTTAATTCACAA
a S V T R N D V G P Y E C G I Q N E L S V -
GACCACAGGACCCAGTCATCCTGAATGTCTCTATGGCCAGACGACCCACCATTTCC
1201 -----+----- 1260
CTGGTGTCCGCTGGGTGAGTACTTACAGGAGATACCGGCTCTGCTGGGTTGGTAAAGG
a D H S D P V I L N V L Y G P D D P T I S -
CCCTCATACACCTATTACCGTCCAGGGGTGAACCTCAGCCTCTCTGCCATGCAGCCTCT
1261 -----+----- 1320
GGGAGTATGTGGATAATGSCAGGTCCCACTTGGAGTCCGAGAGGACGGTACSTCGGAGA
a P S Y T Y Y R P G V N L S L S C H A A S -
AACCCACCTGCACAGTATTCTTGGTGTGATGGGAACATCCAGCAACACACACAAGAG
1321 -----+----- 1380
TTGGGTGGACGTGTCATAAGAACCACTAATACTACCTTGTAGGTCTTGTGTGTCTCTC
a N P P A Q Y S W L I D G N I Q Q H T Q E -
CTCTTTATCTCCAACATCACTGAGAGAACAGCGGACTCTATACCTGCCAGGCCAATAAC
1381 -----+----- 1440
GAGAAATAGAGGTTGTAGTGACTCTTCTGTGCGCTGAGATATGACCGTCCCGTTATTG
a L F I S N I T E K N S G L Y T C Q A N N -

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FIGURE 8 (CONT'D)

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1441 TCAGCCAGTGGCCACAGCAGGACTACAGTCAAGACAATCACAGTCTCTGCGGAGCTSCCC
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1500 AGTGGGTACCGGTGTCGTCCTGATGTCACTTCTGTTAGTGTGACAGACCCCTCGACGGG

a   S A S G H S R T T V K T I T V S A E L F -

1501 AAGCCCTCCATCTCCAGCAACAACCTCCAAACCCGTTGGAGGACAAGGATGCTGTGGCCCTTC
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1560 TTCGGGAGGTAGAGGTGCTTGTGAGGTTTGGGCACCTCCTGTTCTACGACACCGGAAG

a   K P S I S S N N S K P V E D K D A V A F -

1561 ACCTGTGAACCTGAGGCTCAGAACACAACCTACCTGTGGTGGGTAATGCTCAGAGCCTC
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1620 TGGACACTTGGACTCCGAGTCTTGTGTTGGATGGACACCACCATTACAGTCTCGGAG

a   T C E P E A Q N T T Y L W W V N G Q S L -

1621 CCAGTCAGTCCCAGCCTGCAGCTGTCCAATGGCAACAGGACCCCTCAGTCTATTCAATGTC
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1680 GGTCACTCAGCCTCCGACGTGACAGGTTACCTTTGCTCTGGGAGTGAGATTAAGTTACAG

a   P V S F R L Q L S N G N R T L T L F N V -

1681 ACAAGAAATGACGCAAGAGCCTATGTATGTGGAATCCAGAACTCAGTGAGTGCAAAACCGC
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1740 TGTTCTTTACTGCGTTCTCGGATACATACACCTTAGGTCTTGAGTCACTCACGTTTGGCG

a   T R N D A R A Y V C G I Q N S V S A N R -

1741 AGTGACCCAGTCACCCCTGGATGTCTCTATATGGGCCGGACACCCCATCAFTTCCCCCCCA
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1800 TCACTGGGTCAGTGGGACCTACAGGAGATACCCGGCTCTGSGGGTAGTAAAGCGGGGT

a   S D P V T L D V L Y G P D T P I I S F F -

1801 GACTCGTCTTACCTTTTGGGAGCGGACCTCAACCTCTCTCTGCCACTCGGCCTCTAACCCA
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1860 CTGAGCAGAAATGGAAGCCCTCGCCTGGAGTTGAGAGGACGGGTGAGCCGAGATTGGGT

a   D S S Y L S G A D L N L S C H S A S N F -

TCCCCGCACTATTCTTGGCGTATCAATGGGATACCGCAGCAACACACACAAGTTCTCTTT

1861 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1920 AGGGCGCTCATAAGAACCCTAGTTACCCCTATGGCCTGTTGTGTGTTCAGAGBAA

a   S P Q Y S W R I N G I P Q Q H T Q V L F -

1921 ATCGCCAAAATCAGCCCAAATAAACGGGACCTATGCTGTTTTGTCTCTAAGTTGGCT
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
1980 TAGCGGTTTTAGTGGGTTTATTATTGCCCTGGATACGGACAAAACAGAGATTGAACCGA

a   I A K I T P N N N G T Y A C F V S N L A -

1981 ACTGGCCGCAATAATTCATAGTCAAGAGCATCACAGTCTCTGCACTCTGGAACCTCTCCT
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
2040 TGACCGCGGTTATTAAGGTATCAGTTCTCGTAGTGTGACAGACGTAGACCTTAAGAGGA

a   T G R N N S I V K S I T V S A S G T S F -

2041 GGTCTCTCAGCTGGGGCCACTGTGCGCATCATGATTGAGTGGCTGCTTGGGGTTGCTCTG
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
2100 CCAGAGAGTGGACCCCGGTGACAGCGGTAGTACTAACCCTCAGACCAACCCCAACGAGAC

a   G L S A G A T V G I M I G V L V G V A L -

2101 ATATAG ←
----- 2106
TATATC

a   I ←

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INTERNATIONAL SEARCH REPORT

In national Application No

PCT/CA 00/01253

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K39/00 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

MEDLINE, CANCERLIT, LIFESCIENCES, EMBASE, SCISEARCH, EPO-Internal, BIOSIS, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 47271 A (GUO YAJUN) 18 December 1997 (1997-12-18) page 23, line 14 -page 24, line 22	1-3,15, 16
X	RAO V S ET AL: "PARTIAL CHARACTERIZATION OF TWO SUBPOPULATIONS OF T-4 CELLS INDUCED BY ACTIVE SPECIFIC INTRALYMPHATIC IMMUNOTHERAPY IN MELANOMA PATIENTS" PROCEEDINGS AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 27, 1986, page 325 XP000990377 ISSN: 0197-016X the whole document	1,2,16



Further documents are listed in the continuation of box C.



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Date of the actual completion of the international search

16 March 2001

Date of mailing of the international search report

26/03/2001

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INTERNATIONAL SEARCH REPORT

International Application No.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	<p>IRVINE KARI R ET AL: "Recombinant virus vaccination against "self" antigens using anchor-fixed immunogens." CANCER RESEARCH, vol. 59, no. 11, 1 June 1999 (1999-06-01), pages 2536-2540, XP002161590 ISSN: 0008-5472 the whole document</p> <p style="text-align: center;">-----</p>	1-19

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